

## **DEVELOPMENT OF IMMUNOTHERAPEUTIC IMMUNIZATION FOR VIRUS INFECTIONS AND CANCER**

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Vaccines to prevent virus infection have generally been successful in preventing epidemic childhood infections. However, immunization to resolve persisting viral infection or to eradicate cancer cells expressing non-self antigen has proven challenging when naturally induced immune responses have proven insufficient. In many clinical trials, only minimal efficacy has been demonstrated. We have used animal models of persisting infection to study better immunotherapy strategies. In a model of Herpes Simplex infection, infection can be controlled by inducing immune responses in skin rather than muscle, and by biasing those responses to favor T cell responses over antibody, enabling clearance of otherwise lethal infection. In a model of persisting infection with papillomavirus, we have shown that hyper proliferative epithelium expressing papillomavirus proteins secretes cytokines attracting immunoregulatory lymphocytes, and these suppress cytotoxic T cell responses. Local immunosuppression can be overcome by removing inhibitory cytokines, by administering checkpoint blockade inhibitors, or by preventing epithelial proliferation and consequent attraction of regulatory cells. Clinical trials based on these findings, planned or underway, will be discussed.